

**REMARKS**

Claims 11 and 14-20 currently appear in this application. The Office Action of March 3, 2008, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

**Interview Summary**

Applicant's attorney wishes to thank Examiner Kosack for the courtesies extended during the telephone interview of May 21, 2008. During that interview, it was agreed that the reaction of sulfone to sulfoxide in the presence of a salt of peroxomonosulfuric acid proceeded for an unexpectedly short time under relatively mild oxidation conditions. Examiner Kosack said that he would like to see a declaration by an expert in the field attesting to the fact that a two-hour oxidation of sulfone to sulfoxide is unexpected, and that the increased yield from oxidizing a sulfone with such a salt results in better yields because of no decomposition and side reactions.

### Claim Objections

It is respectfully submitted that the common technical feature of the claims is the oxidization of sulfide to sulfones and thence to sulfoxides using salts of peroxomonosulfuric acid, which produces unexpectedly high yields at mild reaction conditions. Therefore, it is respectfully requested that the restriction requirement be withdrawn.

### Art Rejections

Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watanabe et al., WO 01/02378, in view of Patani et al., *Chem. Rev.*, 1996, 3147-3176.

This rejection is respectfully traversed.

This rejection is respectfully traversed. Claim 11 has been amended to recite that the reaction of sulfone to sulfoxide is conducted at a pH of 6 to 10. Support for this amendment can be found in the specification as filed at page 9, lines 4-6.

In the Background section of the present application, Watanabe is discussed at page 1, lines 8-15. In Watanabe, oxidation of the sulfide to the sulfone proceeds relatively rapidly, but oxidation of the sulfone to the sulfoxide proceeds only gradually and sluggishly and requires energetic conditions, such as elevated temperatures and

prolonged reaction times, which may reduce the yield of the desired product.

In Example 3 of Watanabe, page 17, the sulfoxide is prepared from the sulfone of Example 2 by treating the sulfone with hydrogen peroxide at 55-60°C for six hours. After the reaction mixture is cooled to 5°C, the pH is raised to 6 by adding sodium hydroxide, indicating that Watanabe conducts the reaction at a pH below 6. In the presently claimed method, the oxidization of sulfone to sulfoxide takes only two hours and is conducted at about 5°C. The yield shown in Example 1 is 92% of theoretical, indicating that the reaction has substantially gone to completion. From the differences in reaction conditions, clearly, Watanabe does not disclose or suggest the same process as claimed herein.

In the herein claimed process, such as described in Example 1 on page 13, the oxidation reaction to produce the sulfone is conducted at 5°C for approximately two hours. To produce the sulfoxide, the sulfone is reacted with potassium monopersulfate at 20°C for approximately two hours. The yield is 92% of theory. Watanabe, on the other hand, requires temperatures of 55-60°C for six hours to oxidize the sulfone to the sulfoxide. The differences in reaction conditions alone should be sufficient to demonstrate that potassium monopersulfate are not the equivalent of the other oxidizing

agents disclosed in Watanabe, as the potassium monopersulfate oxidizes the sulfur atom far more quickly and efficiently than hydrogen peroxide, and at milder reaction conditions.

Submitted herewith is the declaration of Dr. Shlomi Cohen, declaring that when the pH of the reaction is below 6 the reaction does not go to completion, resulting in poor yield and selectivity. There is no reference in the literature showing this elevated pH for the sulfone to sulfoxide reaction, and the presently claimed method enables the reaction to proceed smoothly at moderate conditions, with high yield and in a short period of time.

With respect to selecting monoperoxysulfuric acid salts as the oxidizing agents, it has been demonstrated that these salts are superior to hydrogen peroxide/water as disclosed in Watanabe, who groups all of the oxidizing agents together as conventional oxidizing agents that could be used. There was no recognition in Watanabe that peroxomonosulfuric acid would be superior in oxidizing thioethers to sulfones and sulfoxides, and particularly in oxidizing the sulfones to sulfoxides, using much milder reaction conditions than in Watanabe.

The CCPA. *In re Antonie*, 559 F.2d 618; 195 USPQ 6 (CCPA 1977) noted that the court has found exceptions to the obvious to try rule in cases where the results of optimizing a

variable, which was known to be result effective, were unexpectedly good. *In re Weymouth*, 499 F.2d 1273, 182 USPQ 290 (CCPA 1974); *in re Saether*, 492 F.2d 849, 181 USPQ 36 (CCPA 1974). In the present application, where the applicant has discovered that monoperoxysulfates are quite superior to other conventional oxidizing agents, there is nothing in Watanabe that makes the claimed process obvious, as Watanabe grouped all oxidizing agents together. It has been demonstrated that the herein claimed process using a monoperoxysulfuric acid is far superior to the Watanabe process, which uses another conventional oxidizing agent, hydrogen peroxide/water.

It is not understood why Patani has been cited, because Patani only discusses the steric properties of substituting hydrogen by fluorine. However, the difference in the electronic effects of a fluorine substituent, fluorine being the most electronegative element in the periodic table, is often the basis for the major differences in pharmacological properties of agents where fluorine has been substituted for hydrogen (Patani, page 3149, left column, last full paragraph). From this, one skilled in the art would assume that substituting fluorine for hydrogen would produce compounds with quite different activities. Because of the huge difference in electronic effects of fluorine substitution compared to hydrogen, no skilled artisan would be able to

predict the same reaction pathway with the molecule substituted with fluorine as compared to hydrogen. Accordingly, Patani adds nothing to Watanabe.

#### **Double Patenting**

Claims 11-20 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claim 6 of Watanabe, U.S. Patent 6,734,198 in view of Patani.

This rejection is respectfully traversed. As noted above, the herein claimed process provides an unexpected solution to the problem of the undesirable oxidation of the butenyl double bond during the oxidation reaction of the sulfur in compounds (I) and (II). This solution is not obvious in view of the disclosure of Watanabe in view of Patani because thereof the much shorter reaction time and the mild reaction conditions.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

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Respectfully submitted,

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